

#### REMARKS

Claims 1-14, 29-31, 33-39, 45-49 and 53 were pending in the present application. Claims 1-3, 12, 45, 47-48 have been amended herein and claim 49 has been canceled herein. Support for amended claim 1 can be found throughout the specification and original claims, such as for example, in original claims 1 and 3. Claims 2, 3, 12, 45, and 47 have been amended herein to correct typographical errors and/or inadvertent omissions. Support for amended claim 48 can be found throughout the specification and original claims, such as for example, in original claim 49. No new matter has been added. Upon entry of the present amendment, claims 1-14, 29-31, 33-39, 45-48, and 53 will be pending.

As a preliminary matter, Applicants thank the Examiner for recognizing the patentability of claims 3-11.

#### I. Rejections under 35 U.S.C. § 112, first paragraph

A. Claims 45-47 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to meet the enablement requirement. Despite acknowledging that compounds of formula IX where R<sub>4</sub> may contain a piperidine, pyrrolyl, pyridine, thiophene, or dioxo are enabled; the Action alleges that the specification provides no guidance as to what other rings might be suitable and there is no basis in the prior art directed to similar compounds having the same activity as herein. See Action at page 3. The Action also alleges that there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will share the same physiological properties since they allegedly are so structurally dissimilar; and alleges that the limited number of examples do not enable the preparation of such a diverse group of compounds embraced by the claims as presently recited. *Id.* at pages 3-4. Applicants respectfully request reconsideration in light of amended claim 45.

Although Applicants believe that original claim 45 is enabled, solely to expedite prosecution and without disclaimer of subject matter, claim 45 has been amended to recite compounds of formula IX, wherein R<sub>4</sub> is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)<sub>n</sub>R<sub>5</sub>, CONR<sub>5</sub>R<sub>6</sub> or SO<sub>2</sub>R<sub>5</sub>.

In view of the foregoing amendment, Applicants respectfully assert that claims 45-47 are enabled, and request that the claim rejection be withdrawn.

**B.** Claims 48 and 49 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Specifically, the Action alleges that the specification does not reasonably provide enablement for treating any disease or condition. The allegation is based on the premise that Applicants have merely provided evidence that a single compound can inhibit TACE, and it would thus require undue experimentation for the artisan to use the compounds as claimed. See Action at page 5. Applicants respectfully request reconsideration in light of the amendments made herein.

Claim 48 has been amended herein to recite specific conditions and disorders for which the role of TACE has been established, and claim 49 has been canceled herein. Further, Applicants have provided an example compound that demonstrates TACE inhibition and have disclosed procedures for measuring the TACE inhibitory activity of other compounds of the invention. While Applicants recognize that the work involved could be voluminous, nothing more than routine skill in the art and Applicants' teachings is required. Even voluminous experimentation is not undue so long as it is of a routine nature. See *Ex parte Forman*, 230 U.S.P.Q. 546, 547 (Pat. Off. Bd. App. 1986). Given the teachings of Applicants' specification, one skilled in the art, could readily determine, through routine experimentation, the TACE inhibitory activity of each of the compounds of the present invention. One skilled in the art would recognize the role of TACE in the recited conditions and disorders. The data in the instant application demonstrates the ability of compounds of the invention to inhibit TACE. Thus, one skilled in the art, armed with the disclosure of the present application, would recognize that the inhibition of TACE, observed with compounds of the present invention, could be used to treat the conditions and disorders described in the claims.

In view of the foregoing discussion, Applicants respectfully assert that the claimed invention meets the requirements of 35 U.S.C. § 112, first paragraph, and request that the claim rejection be withdrawn.

## **II. Rejections under 35 U.S.C. § 112, second paragraph**

**A.** Claim 48 stands rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. In particular, the Action alleges that

defining a disease by its underlying cause renders the scope of the intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. See Action at page 5. Applicants respectfully disagree and assert that claim 48 as presented is clear. However, solely to expedite prosecution and without disclaimer of subject matter, claim 48 has been amended to recite specific conditions and disorders. Accordingly, Applicants respectfully assert that claim 48 meets the requirements of 35 U.S.C. § 112, second paragraph, and request that the claim rejection be withdrawn.

**B.** Claims 1, 2, 12-14, 29-31, 33-39, and 53 stand rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps. Specifically, the Action alleges that there is not recitation of how formula V is converted to formula I, the final product. See Action at page 6. Although Applicants respectfully disagree with the allegation, solely to advance prosecution and without disclaimer of subject matter, claim 1 has been amended herein. Amended claim 1 positively recites the method steps of the claimed process. Further, as discussed in Applicants prior response, the remarks of which are incorporated herein by reference, Applicants have described the step of converting a compound of formula V to a hydroxamic acid derivative of formula I with sufficient clarity and particularity to permit one skilled in the art to understand what the claimed conversion requires. (See pages 22-23 of Applicant Arguments/Remarks Made in an Amendment filed September 17, 2007). "The requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles...Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite." See *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, 71 U.S.P.Q.2d 1081, 1089 (Fed. Cir. 2004). Applicants respectfully assert that one skilled in the art, armed with Applicants' disclosure, would be able to discern the meaning of "converting" as claimed by Applicants.

In view of the foregoing, Applicants respectfully assert that claims 1, 2, 12-14, 29-31, 33-39, and 53 meet the requirements of 35 U.S.C. § 112, second paragraph, and request that the claim rejection be withdrawn.

**III. Conclusion**

In view of the foregoing, Applicants respectfully submit that the pending claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (610) 640-7851 if there are any questions regarding the present application.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to deposit account 50-0436.

Respectfully submitted,

/Nikhil A. Heble, Reg.#61,347/

**Nikhil A. Heble, Pharm.D**

Date: **February 27, 2008**

**Pepper Hamilton LLP**  
400 Berwyn Park  
899 Cassatt Road  
Berwyn, PA 19312  
610.640.7851  
215.827.5279